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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,784	09/15/2003	Fernando Donate	38342-193024	7260

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EXAMINER	
DESAI, ANAND U	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/661,784	DONATE ET AL.	
	Examiner	Art Unit	
	Anand U Desai, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *14-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-13, drawn to an anti-angiogenic polypeptide, in the reply filed on September 16, 2004 is acknowledged. The traversal is on the ground(s) that it would be proper to rejoin the nucleic acid, vector, and transformed cell claims with the elected polypeptide, because the nucleic acid may be considered functionally equivalent to a protective coating or packaging of the active ingredient. This is not found persuasive because the protein of invention I, and the nucleic acid of invention IV are distinct inventions. They are distinct inventions because the protein product can be made by another materially different process, such as by synthetic peptide synthesis or purification from the natural source. In addition, the nucleic acid may be used for processes other than the production of the protein, such as nucleic acid hybridization assay.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 14-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 16, 2004. This application contains claims 14-42 drawn to an invention nonelected with traverse filed on September 16, 2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 1-13 are currently pending and are under examination.

Priority

3. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(e). The priority date is September 13, 2002.

Oath/Declaration

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The U.S. Provisional application number is incorrect. The oath identifies provisional application 60/401,279, but should be identified as 60/410,279. In addition, there is a non-initialed and/or non-dated alteration to the oath. See 37 CFR 1.52(c). The citizenship for Inventor Donate was not initialed and/or dated.

Specification

5. The disclosure is objected to because of the following informalities:

6. The first paragraph should have the cross-reference to related applications. Suggest, "This application claims priority to U.S. Provisional Patent Application Ser. No. 60/410,279, filed on September 13, 2002."

7. The amino acid sequences disclosed are not in compliance with 37 CFR 1.821-1.825. Specifically see 37 CFR 1.822 (d) 1. The amino acids in a protein or peptide sequence shall be listed using the three-letter abbreviation with the first letter as an upper case character, as in WIPO Standard ST.25 (1998), Appendix 2, Table 3. See for example page 10, the two amino acid sequences disclosed.

8. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. On page 12, paragraph 61, there is a hyperlink, http://www.gcg.com.

9. There appears to be a typographical error on page 16, paragraph 74. The citation is preceded by a set of "[???]."

10. On page 17, paragraph 78, there is a right parenthesis missing after the Swiss Prot number.

11. On page 36, paragraph 146, there is a left parenthesis missing before the author, Endo, Y. It appears the reference should be (Endo, Y. et al. ...(1987)).

12. On page 48, paragraph 196, the Gorman, CM reference is missing a right parenthesis after the year. Insert ")."

13. On page 50, paragraph 204, the Miller, DG reference is missing a right parenthesis after the year. Insert ")."

14. On page 51, paragraph 204, the Bank et al. reference is missing a right parenthesis after the year. Insert ")."

15. There appears to be a typographical error for the Berkner, KL reference on page 51, paragraph 206.

16. On page 51, paragraph 206, the Samulski, RJ et al. reference is missing a right parenthesis after the year. Insert ")."

Appropriate correction is required.

Claim Rejections - 35 USC § 112

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 3-7, and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

19. In claim 3, what is a "therapeutic label?"

20. In claims 4-7 is the detectable label the same as the diagnostic label in claim 3? Suggest replacing diagnostic label in claim 3 with "detectable label".

21. Claims 10-13 are rejected for depending on rejected claim 3.

22. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

23. Claim 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is drawn to a variant or derivative thereof of an anti-angiogenic polypeptide having the sequence identified as either SEQ ID NO: 1 or 3. To satisfy the written description requirement, the specification must describe the invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. The specification does not describe the structure, that is amino acids in the various polypeptides that can be altered without affecting the function of a specific polypeptide. For one to be in possession of the

claimed invention, the inventor would have to know the functional consequences of structural alterations. Thus due to the limited predictability in the art, a skilled artisan would not find adequate support for variants and derivatives thereof of an anti-angiogenic polypeptide as disclosed in claim 1 in the specification. Claims 2-13 are rejected for depending on a rejected base claim.

Claim Rejections - 35 USC § 102

24. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

25. Claims 1-3, 8-10, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by McCrae, R. (WO 00/35407). McCrae, R. discloses the inhibition of angiogenesis by high molecular weight kininogen domain 3 peptides. McCrae, R. discloses that peptides containing amino acid sequences Asn(275)-Lys(282), Cys(246)-Cys(249), and Leu(331)-Tyr(338), which are kininogen domain 3 amino acid sequences, can inhibit endothelial cell proliferation and are useful as anti-angiogenic agents (see WO 00/35407, page 14, lines 20-28). McCrae, R. disclose kininogen domain 3 peptides as a pharmaceutical used to inhibit angiogenesis. The therapeutically effective amount of the peptides may be administered as a composition in combination with a pharmaceutical carrier (see WO 00/35407, page 18, lines 11-16). The pharmaceutical composition can be delivered by

injection (see WO 00/35407, page 19, line 20-30, current application, claims 1-3, 8-10, and 13).

26. Claims 1, and 2 are rejected under 35 U.S.C. 102(a) as being anticipated by Zhang et al. (Can. J. Physiol. Pharmacol. 80: 85-90 (2002)). Zhang et al. disclose the inhibition of angiogenesis by two-chain high molecular weight kininogen and kininogen derived polypeptides. Zhang et al. disclose the inhibition of endothelial cell proliferation by two-chain high molecular weight kininogen (see Results section, 1st paragraph, and Table 1). Zhang et al. disclose the inhibition of bFGF- and VEFG-induced angiogenesis in the chorioallantoic membrane assay by two-chain high molecular weight kininogen (see Results section, HKa and HKa D5 inhibit angiogenesis in vivo, and Figure 3). Zhang et al. also discloses the inhibition of endothelial cell proliferation and induction of endothelial cell apoptosis by domain 3 polypeptides of kininogen, corresponding to amino acids 267-282 and 275-290 of kininogen (see Results section, last paragraph, and Figure 5, current application, claims 1, and 2).

Claim Rejections - 35 USC § 103

27. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

28. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

29. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being obvious over McCrae, R. (WO 00/35407) in view of Piwnica-Worms U.S. Patent 6,348,185 B1.

McCrae, R. discloses the inhibition of angiogenesis by high molecular weight kininogen domain 3 peptides. McCrae, R. discloses that peptides containing amino acid sequences Asn(275)-Lys(282), Cys(246)-Cys(249), and Leu(331)-Tyr(338), which are kininogen domain 3 amino acid sequences, can inhibit endothelial cell proliferation and are useful as anti-angiogenic agents (see WO 00/35407, page 14, lines 20-28). McCrae, R. disclose kininogen domain 3 peptides as a pharmaceutical used to inhibit angiogenesis. The therapeutically effective amount of the peptides may be administered as a composition in combination with a pharmaceutical carrier (see WO 00/35407, page 18, lines 11-16). The pharmaceutical composition can be delivered by injection (see WO 00/35407, page 19, line 20-30). McCrae, R. does not disclose a composition wherein the kininogen peptide is labeled with a detectable label.

Piwnica-Worms discloses a composition comprising a peptide, a diagnostic or pharmaceutically active substance, and a linker moiety that links the peptide with a

diagnostic or pharmaceutically active substance. The diagnostic substance is selected from the group consisting of radionuclide, a relaxivity metal, a flourochrome, a dye, and an enzyme substrate. The radioactive isotope is selected from a group consisting of Tc, Ru, In, Ga, Co, Pt, Fe, Os, Ir, W, Re, Cr, Mo, Mn, Rb, Pd, Nb, Cu, and Tu (see U.S. Patent '185, claims 1, 12, and 15). The composition can be administered by injection (see U.S. Patent '185, column 28, line 27, and example 10).

One would have been motivated to bind a radionuclide with the anti-angiogenic polypeptide disclosed by McCrae, R. to detect and treat disorders related to endothelial cell proliferation, and angiogenesis, such as metastatic cancers. Therefore, it would have been obvious to a person having ordinary skill in the art to label the anti-angiogenic polypeptide disclosed by McCrae, R. with a diagnostic or pharmaceutically active substance disclosed by Piwnica-Worms (current application, claims 1-13).

30. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being obvious over Zhang et al. (Can. J. Physiol. Pharmacol. 80: 85-90 (2002)) in view of Piwnica-Worms U.S. Patent 6,348,185 B1.

Zhang et al. disclose the inhibition of angiogenesis by two-chain high molecular weight kininogen and kininogen derived polypeptides. Zhang et al. disclose the inhibition of endothelial cell proliferation by two-chain high molecular weight kininogen (see Results section, 1st paragraph, and Table 1). Zhang et al. disclose the inhibition of bFGF- and VEFG-induced angiogenesis in the chorioallantoic membrane assay by two-chain high molecular weight kininogen (see Results section, HKa and HKa D5 inhibit angiogenesis in vivo, and Figure 3). Zhang et al. also discloses the inhibition of

endothelial cell proliferation and induction of endothelial cell apoptosis by domain 3 polypeptides of kininogen, corresponding to amino acids 267-282 and 275-290 of kininogen (see Results section, last paragraph, and Figure 5). Zhang et al. does not disclose a composition wherein the kininogen peptide is labeled with a detectable label or a therapeutically active moiety.

Piwnica-Worms discloses a composition comprising a peptide, a diagnostic or pharmaceutically active substance, and a linker moiety that links the peptide with a diagnostic or pharmaceutically active substance. The diagnostic substance is selected from the group consisting of radionuclide, a relaxivity metal, a flourochrome, a dye, and an enzyme substrate. The radioactive isotope is selected from a group consisting of Tc, Ru, In, Ga, Co, Pt, Fe, Os, Ir, W, Re, Cr, Mo, Mn, Rb, Pd, Nb, Cu, and Tu (see U.S. Patent '185, claims 1, 12, and 15). The composition can be administered by injection (see U.S. Patent '185, column 28, line 27, and example 10).

One would have been motivated to bind a radionuclide with the anti-angiogenic polypeptide disclosed by Zhang et al. to detect and treat disorders related to endothelial cell proliferation, and angiogenesis, such as metastatic cancers. Therefore, it would have been obvious to a person having ordinary skill in the art to label the anti-angiogenic polypeptide disclosed by Zhang et al. with a diagnostic or pharmaceutically active substance disclosed by Piwnica-Worms (current application, claims 1-13).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U Desai, Ph.D. whose telephone number is (571)

272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen Cochrane Carlson PhD

October 20, 2004

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER